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L17: Entry 2 of 3

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Sep 30, 1988

DERWENT-ACC-NO: 1988-325338

DERWENT-WEEK: 198846

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TITLE: Compsn. for controlling degeneration of skin - contains vitamin=a and cpds. of sulphur, manganese and magnesium

INVENTOR: THOREL, J N

PATENT-ASSIGNEE:

ASSIGNEE

CODE

THOREL J N

THORI

PRIORITY-DATA: 1987FR-0004155 (March 25, 1987), 1987FR-0704155 (March 25, 1987)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
FR 2612775 A	September 30, 1988		009	

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
FR 2612775A	March 25, 1987	1987FR-0704155	

INT-CL (IPC): A61K 7/40; A61K 31/37; A61K 33/04; A61K 35/78

ABSTRACTED-PUB-NO: FR 2612775A

BASIC-ABSTRACT:

Compsn. for preventing or treating degeneration of the skin comprises Vitamin A and physiologically acceptable cpds. of S, Mn and Mg.

Specifically the comps. is based on ascorbic acid (0.1-2 wt.%) and bilberry (vaccinium myrtillus) extract (5-60 wt.%).

USE/ADVANTAGE - The comps. is esp. used to control aging processes, by supplying/reequilibrating necessary vitamins, trace elements and other 'vital stimulants' Ascorbic acid is a potentiator of the plant extract components. Treatment with the comps. results in regularisation of keratinisation and prodn. of sebum; catalyses cellular metabolism and protein synthesis, and stabilises cellular structures.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS: COMPOSITION CONTROL DEGENERATE SKIN CONTAIN VITAMIN=A COMPOUND SULPHUR MANGANESE MAGNESIUM

DERWENT-CLASS: D21 E15

CPI-CODES: D08-B09A; E03; E07-A02B;

CHEMICAL-CODES:

Chemical Indexing M3 \*01\*

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<a href="#">L3</a>	manganese gluconate or manganese carbonate or manganese acetate or manganese citrate or manganese oleate or manganese oxalate	4372	<a href="#">L3</a>
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Chemists

=> s manganese  
L1 386918 MANGANESE

=> s calcium channel or calcium channels  
L2 96424 CALCIUM CHANNEL OR CALCIUM CHANNELS

=> s l1(l)l2  
L3 486 L1(L) L2

=> s l2(p)l2  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L11(P)L11'  
L4 96424 L2(P) L2

=> s l1(p)l2  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L5(P)L11'  
L5 338 L1(P) L2

=> s l1(s)l2  
L6 277 L1(S) L2

=> s l1(5a)l2  
L7 132 L1(5A) L2

=> s cosmetic or wrinkle or wrinkles or cosmetics  
L8 151152 COSMETIC OR WRINKLE OR WRINKLES OR COSMETICS

=> s l8 and l3  
L9 11 L8 AND L3

=> dup rem l9

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L10 11 DUP REM L9 (0 DUPLICATES REMOVED)

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L10 ANSWER 1 OF 11 USPATFULL

TI Manganese compositions for reducing/preventing skin **wrinkles**  
and fine lines

AB A regime/regimen for relaxing and/or slackening human cutaneous and/or  
subcutaneous tissue, in particular for treating **wrinkles** and  
fine lines in the skin, comprising administering to an individual  
subject in need of such treatment, a thus-effective amount. . .

SUMM [0004] The present invention relates to the administration, to  
individuals in need of such treatment, of **cosmetic**  
/dermatological compositions comprising effective amounts of  
**manganese** or salts thereof for relaxing and/or slackening  
cutaneous and/or subcutaneous tissue, notably for reducing/preventing  
**wrinkles** and fine lines in the skin.

SUMM . . . possible and, consequently, to fade out the signs and marks of  
aging of the skin, which are especially reflected in **wrinkles**  
and fine lines. In this respect, advertizing and the fashion world  
report products intended to maintain a radiant and **wrinkle**  
-free skin for as long as possible, which are signs of youthful skin,  
and all the more so since the physical. . .

SUMM [0007] Heretofore, **wrinkles** and fine lines were treated with  
**cosmetic** products containing active agents that act on the skin,  
for example by moisturizing it or by improving cell renewal, or, . . .  
synthesis of collagen, of which skin tissue is composed. However, it

was to date unknown to elicit an effect on **wrinkles** by influencing  
the contractile elements present in the skin.

SUMM . . . spasticity states (see A. Blitzler et al., Arch. Otolaryngol.  
Head Neck Surg., 119, pages 1018 to 1022 (1993)) and on **wrinkles**  
of the glabella, which are the **wrinkles** between the eyebrows  
(see J. D. Carrutgers et al., J. Dermatol. Surg. Oncol., 18, pages 17 to  
21 (1992)). Consequently, it is possible to act on the muscular  
contractile component of **wrinkles** (in particular on the motor  
plate which corresponds to the nerve/muscle junction).

SUMM . . . as the motor neurone. Moreover, the cell membranes of each  
nerve fiber also comprise many ion channels, and in particular  
**calcium channels**, which are capable of allowing the  
corresponding element to permeate in ionic form, which in this  
particular case is calcium.

SUMM . . . better describe the calcium-permeability changes, it is  
currently common to consider that this permeability corresponds to the  
opening of membrane-bound **calcium channels**, these  
channels being operated by variations in the membrane potential (VOC)

or by activation of the membrane-bound receptors (ROC). To date, six VOC  
types of **calcium channel** (L, N, T, P, Q and R) have  
been identified.

SUMM . . . also be appreciated from the foregoing that the contraction or  
hypercontraction of certain facial muscles results in the appearance of  
**wrinkles**. This muscle activation is itself partly induced by a  
variation in calcium flux through the transmembrane **calcium**  
**channels**.

SUMM . . . muscle fiber, which is under the direct control of the  
neuromotor influx, serves an essential function in the formation of

**wrinkles** and that the modulation of the neuromotor influx and the control of the contraction of muscle fibers play an essential role in the formation of **wrinkles**. Thus, it has now been found that the modulation of motor contraction attenuates not only **wrinkles** but also fine lines and also exerts a "smoothing" effect on the skin's microrelief. It has also now been found that cutaneous and subcutaneous tissues comprise **calcium channels**, a hitherto unknown phenomenon.

SUMM [0022] Briefly, the present invention features administering **manganese** values and influencing the **calcium channels** of cutaneous and subcutaneous tissues to relax or slacken same and thus reduce **wrinkles** and fine lines.

SUMM [0025] **Manganese** is a metal which is very widespread at the surface of the earth's crust. It belongs to Group VIIa of the Periodic Table, its atomic number is 25 and its atomic weight is 54.93. **Manganese** has several valences (1 to 7), the divalent and trivalent forms being those that are the most biologically active.

SUMM [0026] **Manganese** is widely used in the metallurgy industry, in the manufacture of dry batteries and as a colorant.

SUMM [0030] **Manganese** has been implicated in many metabolic pathways:

SUMM [0033] (c) immunity, in which **manganese** appears to be necessary for a proper synthesis of antibodies;

SUMM . . . which promotes a reduction in the fertility of females, and of males, may be due to the limiting action of **manganese** on the synthesis of cholesterol and of sexual hormone precursors.

SUMM [0035] Two properties permit explaining certain of the physiopathological roles of **manganese**:

SUMM [0037] **Manganese** is a metal which activates numerous enzymes and lectins. It intervenes either as a dissociable element or by forming

an. . .

SUMM [0038] (2) Its inhibitory activity on **calcium channels**

SUMM [0040] **Manganese** blocks the penetration of calcium into the cytoplasm in many cells exhibiting secretory activity (for example pancreas), or electric activity; in particular, it inhibits the output of neurotransmitters at the motor plate. **Manganese** exerts inhibitory action on the stimulation of B and T lymphocytes, if it is added to the medium, a very. . .

SUMM [0041] In order for a substance to be recognized as a **calcium-channel** inhibitor, also referred to herein as a calcium antagonist, it must be able to reduce the intracellular calcium concentration or. . .

SUMM [0043] **Manganese** and the salts thereof fully satisfy these criteria.

SUMM [0044] As indicated above, the present invention features influencing **calcium channels** to relax or slacken vascular tissues, and thus combating **wrinkles** and fine lines, via administering, to an individual subject in need of such treatment, **manganese**, whether in ionic form, in the form of a salt or in the form of **manganese**-rich natural, plant or microorganism, particularly bacterial, extracts.

SUMM [0045] Thus, this invention features the administration of compositions comprising an effective amount of **manganese** and/or at least one of the salts thereof, to relax and/or slacken cutaneous and/or subcutaneous tissue, such compositions containing a. . .

SUMM . . . acceptable medium therefor, administration of an effective amount of natural, plant or microorganism, particularly bacterial, extracts that are rich in **manganese** or in **manganese**

salt, to relax and/or slacken cutaneous and/or subcutaneous tissue.

SUMM [0047] By the term "**manganese salts**" are intended organic or inorganic **manganese** salts.

SUMM [0048] Exemplary organic salts according to the invention include **manganese** carbonate, **manganese** acetate, **manganese** citrate, **manganese** oleate, **manganese** oxalate, etc.

SUMM [0049] And exemplary inorganic **manganese** salts include the mineral salts, for instance **manganese** chloride, **manganese** borate, **manganese** nitrate, **manganese** phosphate, **manganese** sulfate, etc.

SUMM [0050] Moreover, except where otherwise indicated, the term "**manganese**" means **manganese** which is not only in ionic form but also in the form of salts or in the form of **manganese**-rich natural, plant or microorganism, particularly bacterial, extracts.

SUMM [0052] The present invention also features formulating an effective amount of **manganese** values into physiologically acceptable media to provide compositions suited for smoothing the skin, and also for attenuating and/or eliminating the. . .

SUMM [0053] The subject compositions are well suited for curatively and/or preventively combating **wrinkles** and fine lines in the skin.

SUMM [0054] The subject compositions are particularly well suited for reducing **wrinkles** and fine lines in the skin.

SUMM [0056] Thus, the effective amount of **manganese** which may be administered according to the invention depends on the desired effect and may vary over a wide range.

SUMM [0057] To provide an order of magnitude, it is intended, according to the invention, to administer **manganese** in an amount of from 0.0001% to 10% of the total weight of the composition and preferably in an amount. . .

SUMM [0058] When, according to the invention, a **manganese**-rich natural, plant or microorganism, particularly bacterial, extract is administered, one skilled in this art can easily adapt the amount of extract such that, in the final analysis, the **manganese** is administered in the amounts indicated above.

SUMM [0059] Exemplary **manganese**-rich natural extracts according to the invention include the extracts of nut or extracts of tea.

SUMM [0060] The compositions of the invention are intended for **cosmetic** or dermatological applications. The compositions of the invention are preferably suited for **cosmetic** applications.

SUMM [0061] The regime/regimen according to the invention is **cosmetic**, since intended to modify a person's appearance.

SUMM . . . the composition. The fatty substances and emulsifiers contained in the emulsion are selected from among those conventionally employed in the **cosmetic** or pharmaceutical field.

SUMM . . . bioaffecting active agents. The amounts of these various adjuvants, additives or active agents are those that are conventional in the **cosmetic** or pharmaceutical field, and, for example, range from 0.01% to 20% of the total weight of the composition. Depending on. . .

SUMM . . . compositions of the invention may contain, particularly exemplary are the active agents which have an effect on the treatment of **wrinkles** or fine lines, other than **manganese**, and in particular keratolytic active agents. By the term "keratolytic" is intended an active agent which has desquamating, exfoliant or. . .

SUMM [0073] Exemplary active agents for the treatment of **wrinkles** or fine lines, which the compositions of the invention may contain, include alverine or salts thereof, chlorine-channel openers, hydroxy acids. . . .

SUMM [0078] The present invention also features a **cosmetic** regime/regimen for treating **wrinkles** and/or fine lines, comprising topically applying onto the skin a **cosmetic** composition containing an effective amount of **manganese**, formulated into a physiologically acceptable medium.

SUMM [0079] The **cosmetic** regime/regimen of the invention may be carried out, in particular, by topically applying the **cosmetic** composition as described above, via usual techniques. For example: application of creams, gels, sera, lotions, makeup-removing milks or sunscreen compositions. . . .

DETD [0089] Composition 1: Anti-**wrinkle** care lotion for the face:

Manganese gluconate	1.50%
Antioxidant	0.05%
Preservative	0.30%
Ethanol (solvent)	8.00%
Water qs	100%

DETD [0090] This lotion acts on **wrinkles** during repeated use (application twice daily for one month).

DETD [0093] The gel obtained acts on **wrinkles**. It may be applied daily, morning and evening for one month.

DETD [0095] A rich white cream is obtained, which reduces **wrinkles** and fine lines, and which may be applied daily.

CLM What is claimed is:

. . . slackening cutaneous and/or subcutaneous tissue, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

2. A regime/regimen for curatively and/or preventively treating **wrinkles** and fine lines in the skin, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

3. A regime/regimen for reducing **wrinkles** and fine lines in the skin, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

. . . regime/regimen for smoothing the skin, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

. . . eliminating microrelief in the skin, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

. . . slackening cutaneous and/or subcutaneous tissue, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.



7. A regime/regimen for relaxing and/or slackening cutaneous and/or subcutaneous tissue, and/or for reducing/preventing **wrinkles** and fine lines in the skin, and/or for smoothing the skin, and/or for attenuating and/or eliminating microrelief in the skin, comprising administering to an individual subject in need of such treatment, a **cosmetic**/dermatological composition which comprises a thus-effective amount of **manganese** and/or at least one salt thereof, formulated into a physiologically acceptable vehicle, diluent or carrier therefor.

8. The regime/regimen as defined by claim 7, said **cosmetic**/dermatological composition comprising from 0.0001% to 10% by weight of **manganese**.

9. The regime/regimen as defined by claim 8, said **cosmetic**/dermatological composition comprising from 0.001% to 5% by weight of **manganese**.

10. The regime/regimen as defined by claim 7, said **cosmetic**/dermatological composition comprising **manganese** in ionic state, or a **manganese** salt, or a **manganese**-rich natural, plant or microorganism extract.

11. The regime/regimen as defined by claim 10, said **cosmetic**/dermatological composition comprising at least one inorganic and/or organic **manganese** salt.

12. The regime/regimen as defined by claim 11, said **cosmetic**/dermatological composition comprising at least one of **manganese** gluconate, **manganese** carbonate, **manganese** acetate, **manganese** citrate, **manganese** oleate, and/or **manganese** oxalate.

13. The regime/regimen as defined by claim 11, said **cosmetic**/dermatological composition comprising at least one of **manganese** chloride, **manganese** borate, **manganese** nitrate, **manganese** phosphate, and/or **manganese** sulfate.

14. The regime/regimen as defined by claim 7, comprising topically applying said **cosmetic**/dermatological composition onto the skin of said individual subject.

15. A regime/regimen for influencing **calcium channels** to relax or slacken skin tissue and thus diminish skin **wrinkles** and fine lines, comprising administering to an individual subject in need of such treatment, a thus-effective amount of **manganese** and/or at least one salt thereof.

16. A regime/regimen for influencing **calcium channels** to relax or slacken skin tissue and thus diminish skin **wrinkles** and fine lines, comprising topically applying onto the skin of an individual subject in need of such treatment, a **cosmetic**/dermatological composition comprising a thus-effective amount of **manganese** and/or at least one salt thereof, formulated into a topically applicable, physiologically acceptable vehicle, diluent or carrier therefor.

17. The regime/regimen as defined by claim 7, said **cosmetic**/dermatological composition being formulated for oral administration.

18. The regime/regimen as defined by claim 7, said **cosmetic** /dermatological composition being formulated for injectable administration.

19. The regime/regimen as defined by claim 7, said **cosmetic** /dermatological composition a topically applicable solution, gel, emulsion, cream, oil, milk, makeup, serum, aerosol, vesicular dispersion, or artificial tanning preparation.

20. The regime/regimen as defined by claim 7, said **cosmetic** /dermatological composition further comprising a bioaffecting amount of alverine, a keratolytic agent, a chlorine-channel opener, a hydroxy acid and/or a retinoid.

21. A topically applicable **cosmetic**/dermatological composition suited for influencing **calcium channels** to relax or slacken skin tissue and thus diminish skin **wrinkles** and fine lines, comprising (i) a thus-effective amount of **manganese** and/or at least one salt thereof and (ii) a bioaffecting amount of alverine or salt thereof, a keratolytic agent, a . . .

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                   without answer number. SCAN must be entered on the  
                   same line as DISPLAY, e.g., D SCAN)  
 STD ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,  
                   DT, FS, LN.CNT, INCL, INCLM, INCLS, NCL, NCLM, NCLS,  
                   IC, ICM, ICS, EXF (STD is the default)  
 STD.EX ----- STD for original and latest publication  
 TRIAL ----- AN, TI, INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC,  
                   ICM, ICS

ENTER DISPLAY FORMAT (STD):end

=> d 2 kwic

L10 ANSWER 2 OF 11 USPATFULL

SUMM [0004] The present invention relates to the administration, to  
           individuals in need of such treatment, of **cosmetic**  
           /dermatological compositions comprising effective amounts of  
           **manganese** or salts thereof for treating cutaneous/subcutaneous  
           vascular tissue and thus combating skin pallor.  
 SUMM . . . muscle of the capillaries of the cutaneous blood circulation.  
           The arrival of this action potential results in the opening of  
           **calcium channels** in the cell membrane and thus the  
           appearance of a Ca.sup.2+ current effecting the exocytosis of the  
           noradrenergic vesicles and. . .  
 SUMM . . . activation of adrenergic receptors triggers a sudden increase  
           in the level of cytoplasmic Ca.sup.2+ by means of the opening of  
           **calcium channels** present in the plasma membrane or in  
           the membrane surrounding the stocks of intracellular calcium contained  
           in the endoplasmic reticulum.. . .  
 SUMM . . . which may be associated with stress is partly induced by a  
           variation in the flow of calcium through the transmembrane  
           **calcium channels** of the skin capillaries.

SUMM [0011] Heretofore, no link had been established between the **calcium channels** of the subcutaneous vascular tissue, **manganese** and the pallor following a stress episode, and accordingly, it was never considered to treat these phenomena by influencing the **calcium channels**, in particular via **manganese**.

SUMM [0012] It has now surprisingly and unexpectedly been determined that administration of effective amounts of **manganese** or salts thereof to individuals in need of such treatment, positively affects the **calcium channels** to relax or slacken cutaneous vascular tissues and thus combats skin pallor.

SUMM [0013] More particularly according to the present invention, it is well known that **manganese** is a metal which is very widespread at the surface of the earth's crust. It belongs to Group VIIa of the Periodic Table, its atomic number is and its atomic weight is 54.93. **Manganese** has several valences (1 to 7), the divalent and trivalent forms being those that are the most biologically active.

SUMM [0014] **Manganese** is widely used in the metallurgy industry, in the manufacture of dry batteries and as a colorant.

SUMM . . . of a Mn deficiency have not been determined irrefutably in man, the consequences of deficiencies examined in animals indicate that **manganese** is involved in many metabolic schemes. However, even today, the knowledge regarding the intimate biochemical mechanisms of Mn remains very. . .

SUMM [0018] **Manganese** has been implicated in many metabolic pathways:

SUMM [0021] (c) immunity, in which **manganese** appears to be necessary for a proper synthesis of antibodies;

SUMM . . . which promotes a reduction in the fertility of females, and of males, may be due to the limiting action of **manganese** on the synthesis of cholesterol and of sexual hormone precursors.

SUMM [0023] Two properties permit explaining certain of the physiopathological roles of **manganese**:

SUMM [0025] **Manganese** is a metal which activates numerous enzymes and lectins. It intervenes either as a dissociable element or by forming an. . .

SUMM [0026] (2) Its inhibitory activity on **calcium channels** :

SUMM [0028] **Manganese** blocks the penetration of calcium into the cytoplasm in many cells exhibiting secretory activity (for example pancreas), or electric activity; in particular, it inhibits the output of neurotransmitters at the motor plate. **Manganese** exerts inhibitory action on the stimulation of B and T lymphocytes, if it is added to the medium, a very. . .

SUMM [0029] In order for a substance to be recognized as a **calcium-channel** inhibitor, also referred to herein as a calcium antagonist, it must be able to reduce the intracellular calcium concentration or. . .

SUMM [0031] **Manganese** and the salts thereof fully satisfy these criteria.

SUMM [0032] As indicated above, the present invention features influencing **calcium channels** to relax or slacken vascular tissues, and thus combating wrinkles and fine lines, via administering, to an individual subject in need of such treatment, **manganese**, whether in ionic form, in the form of a salt or in the form of **manganese**-rich natural, plant or microorganism, particularly

bacterial, extracts.

SUMM [0033] Thus, this invention features the administration of compositions comprising an effective amount of **manganese** and/or at least one of the salts thereof, to relax and/or slacken cutaneous and/or subcutaneous vascular tissue and thus to. . .

SUMM [0034] The present invention more particularly features administering an effective amount of **manganese** to re-establish the skin's vascular equilibrium which has been modified after a stress episode. . . . acceptable medium therefor, administration of an effective amount of natural, plant or microorganism, particularly bacterial, extracts that are rich in **manganese** or in **manganese** salt, to relax and/or slacken cutaneous and/or subcutaneous vascular tissue, and thus to combat skin pallor and/or to re-establish the. .

SUMM [0036] By the term "**manganese** salts" are intended organic or inorganic **manganese** salts.

SUMM [0037] Exemplary organic salts according to the invention include **manganese** carbonate, **manganese** acetate, **manganese** citrate, **manganese** oleate, **manganese** oxalate, etc.

SUMM [0038] And exemplary inorganic **manganese** salts include the mineral salts, for instance **manganese** chloride, **manganese** borate, **manganese** nitrate, **manganese** phosphate, **manganese** sulfate, etc.

SUMM [0039] Moreover, except where otherwise indicated, the term "**manganese**" means **manganese** which is not only in ionic form but also in the form of salts or in the form of **manganese**-rich natural, plant or microorganism, particularly bacterial, extracts.

SUMM [0042] Thus, the effective amount of **manganese** which may be administered according to the invention depends on the desired effect and may vary over a wide range.

SUMM [0043] To provide an order of magnitude, it is intended, according to the invention, to administer **manganese** in an amount of from 0.0001% to 10% of the total weight of the composition and preferably in an amount. . . .

SUMM [0044] When, according to the invention, a **manganese**-rich natural, plant or microorganism, particularly bacterial, extract is administered, one skilled in this art can easily adapt the amount of extract such that, in the final analysis, the **manganese** is administered in the amounts indicated above.

SUMM [0045] Exemplary **manganese**-rich natural extracts according to the invention include the extracts of nut or extracts of tea.

SUMM [0046] The compositions of the invention are intended for **cosmetic** or dermatological applications. The compositions of the invention are preferably suited for **cosmetic** applications.

SUMM [0047] The regime/regimen according to the invention is **cosmetic**, since intended to modify a person's appearance.

SUMM . . . the composition. The fatty substances and emulsifiers contained in the emulsion are selected from among those conventionally employed in the **cosmetic** or pharmaceutical field.

SUMM . . . bioaffecting active agents. The amounts of these various adjuvants, additives or active agents are those that are conventional in the **cosmetic** or pharmaceutical field, and, for example, range from 0.01% to 20% of the total weight of the composition. Depending on. . .

SUMM . . . compositions of the invention may contain, particularly  
of exemplary are the active agents which have an effect on the treatment  
of **wrinkles** or fine lines, other than **manganese**, and in  
particular keratolytic active agents. By the term "keratolytic" is  
intended an active agent which has desquamating, exfoliant or. . .

SUMM [0059] Exemplary active agents for the treatment of **wrinkles**  
or fine lines, which the compositions of the invention may contain,  
include alverine or salts thereof, chlorine-channel openers, hydroxy  
acids. . .

SUMM [0064] The present invention also features a **cosmetic**  
regime/regimen for treating **wrinkles** and/or fine lines,  
comprising topically applying onto the skin a **cosmetic**  
composition containing an effective amount of **manganese**,  
formulated into a physiologically acceptable medium.

SUMM [0065] This invention also features a **cosmetic** regime/regimen  
to combat skin pallor, comprising topically applying onto the skin a  
**cosmetic** composition containing an effective amount of  
**manganese**, formulated into a physiologically acceptable medium.

SUMM [0066] This invention more particularly features a **cosmetic**  
regime/regimen to re-establish the skin's vascular equilibrium which  
has  
been modified after a stress episode, also comprising topically  
applying  
onto the skin a **cosmetic** composition containing an effective  
amount of **manganese**, formulated into a physiologically  
acceptable medium.

SUMM [0067] The **cosmetic** regime/regimen of the invention may be  
carried out, in particular, by topically applying the **cosmetic**  
composition as described above, via usual techniques. For example:  
application of creams, gels, sera, lotions, makeup-removing milks or  
sunscreen compositions. . .

DETD [0078] This lotion reduced facial **wrinkles** when repeatedly  
topically applied (application twice daily for one month).

DETD [0080] This gel also reduced **wrinkles**. It should be applied  
daily, morning and evening, for one month.

DETD [0082] The rich white cream thus obtained, which reduces  
**wrinkles** and fine lines, may be applied daily.

CLM What is claimed is:  
. . . combating skin pallor, and/or for restoring vascular equilibrium,  
comprising administering to an individual subject in need of such  
treatment, a **cosmetic**/dermatological composition comprising a  
thus-effective amount of manganese and/or at least one salt thereof,  
formulated into a physiologically acceptable vehicle, diluent. . .

4. The regime/regimen as defined by claim 3, said **cosmetic**  
/dermatological composition comprising from 0.0001% to 10% by weight of  
manganese.

5. The regime/regimen as defined by claim 4, said **cosmetic**  
/dermatological composition comprising from 0.001% to 5% by weight of  
manganese.

6. The regime/regimen as defined by claim 3, said **cosmetic**  
/dermatological composition comprising manganese in ionic state, or a  
manganese salt, or a manganese-rich natural, plant or microorganism  
extract.

7. The regime/regimen as defined by claim 6, said **cosmetic**  
/dermatological composition comprising at least on inorganic and/or  
organic manganese salt.

8. The regime/regimen as defined by claim 7, said **cosmetic** /dermatological composition comprising at least one of manganese gluconate, manganese carbonate, manganese acetate, manganese citrate, manganese oleate, and/or manganese oxalate.

9. The regime/regimen as defined by claim 7, said **cosmetic** /dermatological composition comprising at least one of manganese chloride, manganese borate, manganese nitrate, manganese phosphate, and/or manganese sulfate.

10. The regime/regimen as defined by claim 3, comprising topically applying said **cosmetic**/dermatological composition onto the skin of said individual subject.

11. The regime/regimen as defined by claim 3, said **cosmetic** /dermatological composition being formulated for oral administration.

12. The regime/regimen as defined by claim 3, said **cosmetic** /dermatological composition being formulated for injectable administration.

13. The regime/regimen as defined by claim 3, said **cosmetic** /dermatological composition a topically applicable solution, gel, emulsion, cream, oil, milk, makeup, serum, aerosol, vesicular dispersion, or artificial tanning preparation.

14. The regime/regimen as defined by claim 3, said **cosmetic** /dermatological composition further comprising a bioaffecting amount of alverine, a keratolytic agent, a chlorine-channel opener, a hydroxy acid and/or a retinoid.

15. A topically applicable **cosmetic**/dermatological composition suited for relaxing and/or slackening cutaneous and/or subcutaneous vascular tissue and for combating skin pallor, and/or for restoring vascular.

=> d 3 kwic

L10 ANSWER 3 OF 11 USPATFULL

DETD . . . growth, fertility, maturation, or other characteristic in specific agricultural products, including animals or plants. They may

be useful in creating **cosmetic** products, fragrances, food preservatives, or nutritional supplements. Thus, the invention provides powerful methods for systematically performing high throughput screens of. . .

DETD . . . be screened as well, as can potentially biologically active ions such as metal ions, e.g., copper, iron, silver, zinc, magnesium, **manganese**, calcium, and gold ions.

DETD . . . Podophyllotoxin and paclitaxel are both microtubule stabilizers

that arrest cells in mitosis, dipyrindamole is an anti-platelet agent, bepridil is a **calcium channel** blocker, and promethazine is an H1 histamine receptor antagonist and is also used as a CNS depressant and anticholinergic agent.. . .

=> d 3 ibib abs

L10 ANSWER 3 OF 11 USPATFULL

ACCESSION NUMBER: 2002:32190 USPATFULL  
TITLE: Methods for identifying combinations of entities as  
therapeutics  
INVENTOR(S): Stockwell, Brent R., Boston, MA, UNITED STATES  
Borisys, Alexis, Boston, MA, UNITED STATES  
Foley, Michael A., Chestnut Hill, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002019011	A1	20020214
APPLICATION INFO.:	US 2001-815429	A1	20010322 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-611835, filed on 7 Jul 2000, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	CLARK & ELBING LLP, 176 FEDERAL STREET, BOSTON, MA, 02110-2214		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Page(s)		
LINE COUNT:	1319		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features a method of screening two-entity or higher order combinations for biological activity using combinational arrays. The method includes the steps of: (a) providing the entities, (b) creating an array of combinations of entities, (c) providing a test element that includes one or more distinct biological moieties, (d) contacting the array of combinations of entities with the test element under conditions that ensure that each entity/test element contacting is segregated from the others, (e) detecting or measuring a property of the test element, and (f) identifying combinations of entities that cause an effect on the property of the test element that is different from the effect of an entity of the combination by itself.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 4 kwic ibib abs

L10 ANSWER 4 OF 11 USPATFULL

DETD . . . growth, fertility, maturation, or other characteristic in specific agricultural products, including animals or plants. They may be useful in creating **cosmetic** products, fragrances, food preservatives, or nutritional supplements. Thus, the invention provides powerful methods for systematically performing high throughput screens of. . .

DETD . . . be screened as well, as can potentially biologically active ions such as metal ions, e.g., copper, iron, silver, zinc, magnesium, **manganese**, calcium, and gold ions.

DETD . . . Podophyllotoxin and paclitaxel are both microtubule stabilizers that arrest cells in mitosis, dipyridamole is an anti-platelet agent, bepridil is a **calcium channel** blocker, and promethazine is an H1 histamine receptor antagonist and is also used as



a CNS depressant and anticholinergic agent.. . . .  
 ACCESSION NUMBER: 2002:32189 USPATFULL  
 TITLE: Methods for identifying combinations of entities as  
 therapeutics  
 INVENTOR(S): Stockwell, Brent R., Boston, MA, UNITED STATES  
 Borisy, Alexis, Boston, MA, UNITED STATES  
 Foley, Michael A., Chestnut Hill, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002019010	A1	20020214
APPLICATION INFO.:	US 2001-815417	A1	20010322 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-611835, filed on 7 Jul 2000, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	CLARK & ELBING LLP, 176 FEDERAL STREET, BOSTON, MA, 02110-2214		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Page(s)		
LINE COUNT:	1307		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention features a method of screening two-entity or higher order combinations for biological activity using combinational arrays. The method includes the steps of: (a) providing the entities, (b) creating an array of combinations of entities, (c) providing a test element that includes one or more distinct biological moieties, (d) contacting the array of combinations of entities with the test element under conditions that ensure that each entity/test element contacting is segregated from the others, (e) detecting or measuring a property of the test element, and (f) identifying combinations of entities that cause an effect on the property of the test element that is different from the effect of an entity of the combination by itself.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 09:13:58 ON 11 JUL 2002)

FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE, KOSMET' ENTERED AT 09:14:10 ON 11 JUL 2002

L1 386918 S MANGANESE  
 L2 96424 S CALCIUM CHANNEL OR CALCIUM CHANNELS  
 L3 486 S L1(L)L2  
 L4 96424 S L2(P)L2  
 L5 338 S L1(P)L2  
 L6 277 S L1(S)L2  
 L7 132 S L1(5A)L2  
 L8 151152 S COSMETIC OR WRINKLE OR WRINKLES OR COSMETICS  
 L9 11 S L8 AND L3  
 L10 11 DUP REM L9 (0 DUPLICATES REMOVED)

=> l8 and l5

L8 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s l8 and l5

L11 3 L8 AND L5

=> dup rem l11

DUPLICATE IS NOT AVAILABLE IN 'KOSMET'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L11

L12 3 DUP REM L11 (0 DUPLICATES REMOVED)

=> d ibib abs

L12 ANSWER 1 OF 3 USPATFULL

ACCESSION NUMBER: 2002:48063 USPATFULL

TITLE: Manganese compositions for reducing/preventing skin  
**wrinkles** and fine lines

INVENTOR(S): Nonotte, Isabelle, Paris, FRANCE  
Breton, Lionel, Versailles, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002028254	A1	20020307
APPLICATION INFO.:	US 2001-859384	A1	20010518 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	FR 2000-6373	20000518
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Norman H. Stepno, Esquire, BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404	
NUMBER OF CLAIMS:	21	
EXEMPLARY CLAIM:	1	
LINE COUNT:	592	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A regime/regimen for relaxing and/or slackening human cutaneous and/or subcutaneous tissue, in particular for treating **wrinkles** and fine lines in the skin, comprising administering to an individual subject in need of such treatment, a thus-effective amount of manganese and/or at least one organic and/or inorganic salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 2 ibib abs

L12 ANSWER 2 OF 3 USPATFULL

ACCESSION NUMBER: 2002:42981 USPATFULL

TITLE: Manganese compositions for treating skin vascular  
tissue and combating skin pallor

INVENTOR(S): Nonotte, Isabelle, Paris, FRANCE  
Breton, Lionel, Versailles, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002025345	A1	20020228
APPLICATION INFO.:	US 2001-859392	A1	20010518 (9)

	NUMBER	DATE
	-----	-----
PRIORITY INFORMATION:	FR 2000-6374	20000518
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Norman H. Stepno, Esquire, BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404	
NUMBER OF CLAIMS:	15	
EXEMPLARY CLAIM:	1	
LINE COUNT:	476	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB	A regime/regimen for relaxing and/or slackening human cutaneous and/or subcutaneous vascular tissue and for combating skin pallor, and/or for restoring stress-modified vascular equilibrium, comprising administering to an individual subject in need of such treatment, a thus-effective amount of manganese and/or at least one organic and/or inorganic salt thereof.	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 3 ibib abs

L12 ANSWER 3 OF 3 USPATFULL  
 ACCESSION NUMBER: 1999:150697 USPATFULL  
 TITLE: Ratite extracts as therapeutic agents  
 INVENTOR(S): Cardinale Fezler, Donna L., Rte. 1, Box 97B, Jacksonville, IL, United States 62650

	NUMBER	KIND	DATE
	-----	-----	-----
PATENT INFORMATION:	US 5989594		19991123
APPLICATION INFO.:	US 1997-907794		19970808 (8)

	NUMBER	DATE
	-----	-----
PRIORITY INFORMATION:	US 1996-24152P	19960809 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Witz, Jean C.	
LEGAL REPRESENTATIVE:	Fishel, Grace J.	
NUMBER OF CLAIMS:	6	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	2214	
AB	Adenosine triphosphate (ATP) deficiency is the cause of many autoimmune, muscle and bone wasting disorders in humans and animals. Ratite muscle and bone extracts provide a rich source of ATP and regulatory proteins which can be used in treating conditions associated with ATP deficiency.	

=> d 3 kwich

'KWICH' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'

The following are valid formats:

The default display format is STD.

ABS ----- AB  
ALL ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,  
RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,  
DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,  
INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,  
EXF, ARTU  
ALLG ----- ALL plus PAGE.DRAW  
BIB ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD, RLI,  
PRAI, DT, FS, EXNAM, LREP, CLMN, ECL, DRWN, LN.CNT  
BIB.EX ----- BIB for original and latest publication  
BIBG ----- BIB plus PAGE.DRAW  
BROWSE ----- See "HELP BROWSE" or "HELP DISPLAY BROWSE". BROWSE must  
entered on the same line as DISPLAY, e.g., D BROWSE.  
CAS ----- OS, CC, SX, ST, IT  
CBIB ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PRAI, DT, FS  
DALL ----- ALL, delimited for post-processing  
FP ----- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI, RLI,  
PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL,  
NCLM, NCLS, EXF, REP, REN, ARTU, EXNAM, LREP,  
CLMN, DRWN, AB  
FP.EX ----- FP for original and latest publication  
FPALL ----- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI,  
RLI, PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL, NCLM,  
NCLS, EXF, REP, REN, ARTU, EXNAM, LREP, CLMN, DRWN, AB,  
PARN, SUMM, DRWD, DETD, CLM  
FPBIB ----- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI,  
RLI, PRAI, REP, REN, EXNAM, LREP, CLM, CLMN, DRWN  
FHITSTR ----- HIT RN, its text modification, its CA index name, and  
its structure diagram  
FPG ----- FP plus PAGE.DRAW  
GI ----- PN and page image numbers  
HIT ----- All fields containing hit terms  
HITRN ----- HIT RN and its text modification  
HITSTR ----- HIT RN, its text modification, its CA index name, and  
its structure diagram  
IABS ----- ABS, indented with text labels  
IALL ----- ALL, indented with text labels  
IALLG ----- IALL plus PAGE.DRAW  
IBIB ----- BIB, indented with text labels  
IBIB.EX ----- IBIB for original and latest publication  
IBIBG ----- IBIB plus PAGE.DRAW  
IMAX ----- MAX, indented with text labels  
IMAX.EX ----- IMAX for original and latest publication  
IND ----- INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,  
EXF, ARTU, OS, CC, SX, ST, IT  
ISTD ----- STD, indented with text labels  
KWIC ----- All hit terms plus 20 words on either side  
MAX ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,  
RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,  
DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,  
INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,  
EXF, ARTU OS, CC, SX, ST, IT  
MAX.EX ----- MAX for original and latest publication  
OCC ----- List of display fields containing hit terms  
SBIB ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,  
DT, FS, LN.CNT

SCAN ----- AN, TI, NCL, NCLM, NCLS, IC, ICM, ICS (random display  
without answer number. SCAN must be entered on the  
same line as DISPLAY, e.g., D SCAN)

STD ----- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,  
DT, FS, LN.CNT, INCL, INCLM, INCLS, NCL, NCLM, NCLS,  
IC, ICM, ICS, EXF (STD is the default)

STD.EX ----- STD for original and latest publication

TRIAL ----- AN, TI, INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC,  
ICM, ICS

ENTER DISPLAY FORMAT (STD):end

=> d 3 kwic

L12 ANSWER 3 OF 3 USPATFULL

DETD . . . heavy metal toxicity site in the cell, upsetting normal  
regulation of the cellular flux of calcium (127) by acting as  
**calcium channel** blockers (93). Metals such as cobalt,  
magnesium, **manganese**, nickel, cadmium, and lead interact and  
block **calcium channels**. There is evidence that  
calmodulin as a calcium binding protein may be targets of heavy metals,  
or may serve to. . .

DETD 20. Zemstov A, Gaddis, M, Montalvo-Lugo, V. **Cosmetic** and  
Moisturizing Properties of Emu Oil: A Pilot Double-Blind Study. 88th  
AOCS Annual Meeting & Expo Abstracts. American Oil Chemists'. . .

=> logy

LOGY IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

29.76

29.97

STN INTERNATIONAL LOGOFF AT 09:19:16 ON 11 JUL 2002